Human Milk as a Source of Methylmercury Exposure in Infants

Philippe Grandjean, Poul J. Jørgensen, and Pál Weihe

¹Institute of Community Health, Odense University, Denmark; ²Department of Clinical Chemistry, Odense University Hospital, Denmark; ³Landssjukrahusid, Tórshavn, Faroe Islands

The neurotoxicity of methylmercury has been demonstrated by serious poisoning episodes. Although the most severe toxicity was apparently due to prenatal methylmercury exposure, poisoning cases in Minamata were also documented in infants who had been exposed to methylmercury only after birth (1). In Iraq, human milk was the suspected source of methylmercury exposure of several poisoned infants (2). Human milk contains mercury, partly in the form of methylmercury, and the mercury concentration in milk is proportional to that in maternal blood (3-5). Experimental evidence in rodents suggests that considerable transfer of mercury to pups may occur through milk from methylmercury-exposed dams (6,7). However, the public health significance of methylmercury transfer through human milk is unclear.

The retention of methylmercury in humans is reflected by the mercury concentrations in scalp hair (8). Mercury concentration profiles in hair from adult poisoning victims suggest an average elimination halflife of 70 days after cessation of methylmercury exposure (3). In nursing mothers, the half-life may be as short as 45 days (2), perhaps due to considerable excretion of mercury in the milk. In a small number of infants exposed to methylmercury in utero during the poisoning episode in Iraq, postnatal decrease of mercury concentrations in hair was very slow; this slow decrease was thought to be due to continued exposure from the milk (9).

According to experimental studies, methylmercury elimination depends on the presence of demethylating bacteria in the gut (10,11). These bacteria tend to become established after weaning and then metabolize methylmercury from the bile into mercuric ions that are eliminated with the feces; unconverted methylmercury is reabsorbed from the gut. Thus, as long as the infant is nursing, mercury elimination is likely to be limited. In vitro studies have demonstrated that demethylation may also occur by the action of rat liver microsomes (12), but whether similar reactions occur in humans is unknown.

Evidence from poisoning episodes (8) and a small population study in New

Zealand (13) suggests that methylmercury exposure may cause neurobehavioral damage to the fetus at exposures corresponding to a maternal hair mercury level above about 10 µg/g. In some fishing communities, this limit may be exceeded, as recorded in the Faroe Islands where the mercury concentrations in maternal hair or in umbilical cord blood were above the safe limit in approximately one out of every five births (14). The Faroe Islands are located in the North Atlantic between Scotland and Iceland, and the population of about 45,000 relies to a large extent on seafood, including pilot whale, which has a high mercury concentration. If the meat from locally caught whales was evenly distributed to the whole Faroese population, the annual catch would, during some years, represent a mercury intake above the World Health Organization/Food and Agriculture Organization (WHO/FAO) provisional tolerable weekly intake (PTWI) for the whole population (15).

Thus, the available evidence suggests that mercury transfer from human milk may be of relevance, but its toxicokinetic behavior in small children is poorly known. Due to the neurotoxic potential of methylmercury, these factors may be of importance for risk assessments. We therefore conducted a study of mercury burdens at about 12 months of age in Faroese children that had been breast-fed for different lengths of time or not at all.

A cohort was identified from consecutive deliveries from 1 March 1986 to the end of 1987 at all three Faroese hospitals in Tórshavn, Klaksvik, and Suderoy. During the active sampling period, we obtained questionnaire data and samples of umbilical cord blood and maternal hair for mercury analysis from 1022 singleton births (75.1% of all deliveries) (14). (One mother first included in the cohort was not a permanent resident of the Faroe Islands and was subsequently excluded.) The study protocol was approved by the regional ethical review committee.

As an integral part of the Faroese health care system, families with small children are visited by district health nurses. For children belonging to the birth cohort, the

As methylmercury is excreted in human milk and infants are particularly susceptible to toxicity due to this compound, the purpose of this study was to evaluate the possible transfer of methylmercury to infants via breast-feeding. In a community with a high intake of seafood, 583 children from a birth cohort were followed. The duration of nursing was recorded, and hair samples were obtained for mercury analysis at approximately 12 months of age. The hair mercury concentrations increased with the length of the nursing period, and those nursed throughout the first year showed the highest geometric mean (9.0 nmol/g or 1.8 µg/g). Human milk therefore seems to be an important source of methylmercury exposure in infants. An increasing time interval from weaning to hair sample collection was not associated with any detectable decrease in mercury concentrations. A slow or absent elimination of methylmercury during the first year after birth could explain this finding. In certain fishing communities, infants nursed for long periods may be at increased risk of developing methylmercury toxicity. Key words: breast-feeding, environmental pollution, hair analysis, mercury poisoning, nutrition, toxicokinetics. Environ Health Perspect 102:74-77(1994)

nurses filled out a questionnaire on developmental data and, at about 1 year of age, a hair sample was collected. Breast-feeding was separated into two periods: one in which the infant received maternal milk only, and a subsequent period where formula and/or baby food was added to the diet.

We obtained questionnaire information and a hair sample sufficient for analysis from 583 children (57.0% of the cohort). Hair samples of at least 100 mg were cut with a pair of scissors close to the root in the occipital area of the head; the hair was tied with a plastic clamp and saved in a small, marked plastic bag. For 557 children (95.6%), hair collection took place at 12 months of age; the rest of the samples (N = 26) were collected about 1–2 months before or after this date, depending on the scheduling of the nurse's visits. The length of the hair collected was gener-

Address correspondence to P. Grandjean, Institute of Community Health, Winsløwparken 17, 5000 Odense C, Denmark.

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ally 2-3 cm, and the sample was analyzed in toto.

The children included in the study were mainly characterized by their residence in districts served by nurses and the willingness and need of the mother to receive the nurse at home during the first year after the child's birth. Thus, the children may not necessarily reflect the average for the Faroe Islands. No district health nurse was available at Suderoy during the study period, and the coverage in the Tórshavn area was incomplete (36.6%) as compared to other districts where questionnaire data and hair samples were obtained from 432 (78.3%) of the children. Based on mercury concentrations in maternal hair at the time of delivery, the prenatal mercury exposures were slightly higher in the children who were visited by a nurse during the first year of life than in those who were not (Table 1). This difference can be explained by the higher intake of whale meat outside Tórshavn.

To determine mercury concentrations in the children's hair, we placed an accurately weighed hair sample of 0.01-0.1 g in a poly(tetrafluoroethylene)-lined digestion vessel before microwave digestion and preparation as described by Pineau et al. (16). Mercury analysis in duplicate was performed by flow-injection cold-vapor atomic absorption spectrometry (Perkin-Elmer model 5100 with FIAS-200 and AS-90). The detection limit for the dissolved sample was estimated to be 0.20 µg/l, i.e., three times the standard deviation of the blank. The total analytical imprecision was estimated to be 12.2, 6.8, and 4.6% at mercury concentrations of 0.24, 0.66, and 11.9 µg/g, respectively. The accuracy of the mercury determinations in human hair

was ensured by using the certified reference material CRM 397 (BCR, Brussels, Belgium) and powdered hair HH-1 (IAEA, Vienna, Austria) (17) as quality control materials; the mercury concentrations of these samples averaged 11.9 μ g/g and 1.6 μ g/g, respectively (assigned values, 12.3 \pm 0.5 μ g/g and 1.7 μ g/g). All results were converted to SI units, where 1.0 μ g = 5.0 nmol.

All mercury concentration data conformed with a Gaussian distribution after logarithmic transformation. Other parameters required the use of nonparametric statistical methods. Nursing periods were split approximately according to the quartiles, and dummy variables were made for the regression analyses. We performed all calculations using SPSS-PC software (Chicago).

The mercury concentration in the infants' hair showed a geometric mean of 5.5 nmol/g and a maximum of 44.1 nmol/g. The mercury concentration in the infant hair correlated with that in maternal hair at the time of delivery (r = 0.38, p <0.0001) and with that in umbilical cord blood (r = 0.41, p < 0.0001) (logarithmic transformations). Results from Japan (18) suggest that, at the time of birth, the mercury concentration in the hair of the baby would probably be similar to that of the mother. In this study, however, the concentration in the child's hair at 1 year of age was only about 25% (geometric mean) of that of the mother at the time of delivery. A total of 79 of the maternal hair samples (13.6%) contained a mercury concentration above the 50 nmol/g (10 µg/g) limit, but the mercury concentration in hair from these children at 1 year of age showed a geometric mean of only 9.1 nmol/g, the mean ratio between the mer-

cury concentrations in child and mother being 0.13.

Most of the infants (97.4%) were nursed for at least a month. Fifteen were not nursed at all. Human milk was the sole source of nutrition for a median of 4 months; 18 children (3.1%) were fed human milk exclusively for more than 6 months. At 12 months, 160 children (27.4%) were still being nursed, but all of these children also received other food at that time. The median time interval from the full termination of breast-feeding to the collection of the hair sample (weaning-sampling interval) was 5 months.

For quartile groups of nursing periods, the mercury concentrations of the infants' hair are shown in Table 2. Those nursed throughout the first year showed the highest geometric mean (9.0 nmol/g). For comparison, those children not nursed at all (N = 15) showed a geometric mean of 3.0 nmol/g.

Both the period where nursing was the only source of nutrition and the period where human milk was supplemented with other food contributed to the mercury concentration in the child's hair (Fig. 1). In a multiple regression analysis where the logarithm of the mercury concentration was the dependent variable, breast-feeding without supplements for at least 4 months was a significant predictor (Table 3). Adjustment for the length of continued nursing with supplementary food caused only small changes in the regression coefficients (Table 3). The total duration of the breast-feeding period was not a better predictor than the period where no supplement was given.

The correlation with nursing time could, at least in part, be due to an effect of the milk diet on the infant's ability to excrete methylmercury, as suggested above. According to this hypothesis, elimination of methylmercury previously absorbed would then begin to increase during the weaning-sampling interval. The weaningsampling time interval was therefore entered as an independent parameter in the multiple regression analyses (Table 3). The regression coefficients for this parameter were relatively small and barely reached statistical significance. However, the inverse relationship between the weaningsampling interval and the duration of breast-feeding makes these calculations difficult to interpret.

A similar analysis was therefore conducted using the data for the 239 children who had been nursed for no more than 5 months, as the length of breast-feeding was only weakly associated with the mercury concentration in hair in this subgroup at 1 year of age (geometric mean, 3.6 nmol/g) (Fig. 1). All but 11 of the hair samples

Table 1. Maternal hair-mercury concentration (nmol/g) at the time of delivery

	Child visited during first year		Child not visited		
District	Number	Geometric mean	Number	Geometric mean	$ ho^b$
Tórshavn	151	17.2	263	15.6	0.26
Suderoy	0	_	55	43.6	_
Other	430	24.4	120	20.6	0.03
Total	581	22.3	438	19.1	<0.01

^aMercury concentration of maternal hair was available for 1019 of the 1022 cohort members.

Table 2. Mercury concentration in hair from infants at approximately 12 months of age in relation to quartiles of the duration of breast-feeding^a

Length of nursing	No.	Mercury concentration (nmol/g)		
(months)	of samples	Geometric mean	Interquartile range ^b	
0–3	143	3.6	2.3–5.7	
4–6	137	4.3	2.7-6.9	
7–11	143	6.1	4.1–10.2	
≥12	160	9.0	5.7-13.7	
All	583	5.5	3.3-9.4	

^aPearson's correlation coefficient between nursing time and hair mercury, r = 0.47; p < 0.0001. ^b25th–75th percentiles.

^bComparison of the two groups by Student's t-test.

Table 3. Regression coefficients for nursing periods (without supplements) of increasing length, as compared to no breast-feeding, with the logarithm of mercury in hair (μmol/g) at 1 year of age as the dependent variable^a

	Duration of nursing without supplements			
Adjustment	1–3 months	4–5 months	≥6 months	
None	0.088	0.301***	0.396***	
Prenatal exposure ^b	0.063	0.284***	0.388***	
Continued nursing with supplements ^c	0.081	0.216***	0.285***	
Weaning-sampling interval	0.078	0.173**	0.206**	
All of the above	0.049	0.161*	0.220***	

^aAdjustment for possible confounders was obtained by including them as independent variables.

were obtained at 12 months of age. As expected, the mercury concentration in the hair of these infants strongly correlated with the mercury concentrations in both maternal hair (r = 0.40, p < 0.0001) and cord blood (r = 0.49, p < 0.0001) (logarithmic transformations). However, it remained independent of the weaning-sampling time interval (Spearman's $r_s = -0.06$; p = 0.35) (Fig. 2). No elimination half-life could therefore be estimated.

The duration of nursing was not related to prenatal mercury exposure. Accordingly, adjustment for maternal hair mercury concentration at delivery produced only small changes in the regression equations (Table 3). Finally, the regression analyses showed almost identical results when carried out only for the slightly smaller group of 432 children from the districts with the most complete sampling (data not shown).

The high methylmercury exposure in the Faroe Islands is due to the seafood diet, especially the consumption of pilot whale meat (14). The average mercury concentration in whale meat is about 3 µg/g, half of which is in the form of methylmercury (15). The group of children studied is not quite a representative sample from the original birth cohort (Table 1). However, findings based on the children that constitute 57% of the cohort are similar to those seen in the subgroup that represents 78% of the children born to mothers residing in the northern islands. Thus, selection factors do not appear to affect the toxicokinetic patterns revealed in this study, and the increased mercury retention in the infant related to breast-feeding could reflect a general pattern.

The mercury concentration in a child's hair at 1 year of age was much lower than that in the maternal hair at the time of delivery. As the mercury concentration in the newborn is expected to match the mercury concentration in the mother's hair (18), a considerable decrease must have taken place. During the first year, the weight of the infants tripled, and the expanded distribution space may have contributed to this decrease. Also, increases in

hair growth rate (19) and changes in hair structure during infancy (20) may have played a role. The relative significance of these factors is unknown at present, and methylmercury retention in the infants can therefore only be evaluated on a relative scale

Compared to mercury concentrations in the hair of 1-year-old children who had not been nursed, the concentration doubled when breast-feeding lasted at least 6 months, and a three-fold increase occurred in those nursed throughout the first year of life (Table 2, Fig. 1). The length of nursing was independent of the maternal mercury burden. Accordingly, the increased retention of methylmercury in the infants who were breastfed for the longest period must be due to increased uptake and/or decreased excretion of this compound.

Mercury concentrations in human milk correspond to about 8% of the concentration in whole blood (3,4), but some of the mercury occurs as mercuric ions (2,5). As the median cord blood mercury concentration is about 120 nmol/l (24 µg/l) in the Faroese cohort (14), an average concentration in milk of about 10 nmol/l (2 µg/l) would be expected. Limited analyses are in general agreement with this calculation (unpublished data). The safety of methylmercury exposure from human milk can be estimated from the WHO/FAO PTWI limit of 0.3 mg of total mercury for an adult, i.e., a daily dose of about 0.6 µg per kg body weight. The average milk intake during the nursing period is about 125 ml/kg body weight/day (21). Without taking into account possible differences in susceptibility to methylmercury exposure, the PTWI would then correspond to a milk

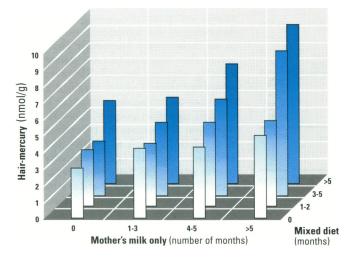


Figure 1. Mercury concentration in hair of 583 12-month-old infants in relation to the length of the nursing period. The mercury concentrations are given as geometric means. The duration of breast-feeding has been separated into the period where breast milk constituted the full diet (horizontal scale) and the period where the diet included other food (right-hand scale). Each of these periods has been split into four groups according to the quartiles.

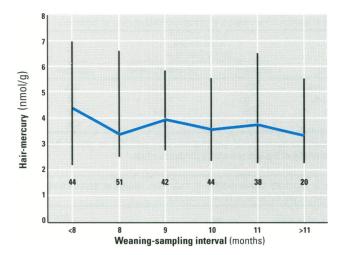


Figure 2. Mercury concentration in hair of 12-month-old infants who had been nursed no more than 5 months in relation to the time interval between weaning and hair sample collection. The mercury concentrations are shown as geometric means and interquartile ranges. The number of children in each group is given below the bar.

 $^{^{\}it b}$ Logarithm of mercury concentrations in umbilical cord blood and in maternal hair.

^cSeparated into three dummy variables according to the quartiles.

^{*}p<0.05; **p<0.01; and ***p<0.001, when compared to 0 months.

mercury concentration of 24 nmol/l (4.8 µg/l). The data on maternal blood-mercury concentrations in the Faroes (14) suggest that this limit will be exceeded in one out of eight mothers in the Faroe Islands. Published data on mercury in human milk include averages of 3 µg/l (15 nmol/l) in Sweden (5), 3.6 µg/l (18 nmol/l) in Japan (18), and 7.6 µg/l (38 nmol/l) in coastal Alaska (22). In Italy (23) and Slovenia (24), single samples of human milk have shown mercury concentrations above the level corresponding to the PTWI. Thus, in several parts of the world, infants may be exposed to considerable amounts of mercury through human milk.

Although adults can eliminate methylmercury after intestinal demethylation, infants may not have this ability due to the absence of demethylating bacteria in the gut (10,11). Exactly when such bacteria colonize the gut is unknown, and interindividual variation could be considerable. Also, although liver microsomes may well induce demethylation (12), the possible significance of this potential in infants is unclear. Had the Faroese infants been capable of demethylating the methylmercury, in particular after weaning, then elimination of methylmercury would presumably have been reflected in the mercury concentrations. A decrease in mercury concentration of hair should then be apparent as a function of the time interval from weaning to hair sampling (Fig. 2). The regression analyses failed to document any change in mercury in hair in relation to time intervals from 7 to 12 months.

In interpreting this finding, two caveats must be considered. While seafood would not normally be included in baby food, some infants may have received small, though probably insignificant, amounts of methylmercury from sources other than human milk. More importantly, account must be taken of the fact that the hair strands analyzed were generally 2-3 cm long. With a hair growth rate of 0.5-1 cm per month (19), each sample represented a period of approximately 3-4 months before hair sampling. Nonetheless, an elimination half-life of 70 days, as seen in adults (3), would be extremely unlikely, given the data shown in Figure 2.

Thus, the findings of this study could be explained by a considerable absorption of methylmercury from human milk and a slow or absent elimination of this compound during the first year of life. These toxicokinetic factors are of considerable importance in the risk assessment for methylmercury. Although prenatal exposures seem most dangerous, continued exposure to methylmercury during the early postnatal period can adversely affect the nervous system (1,2,8). However, the

dose-response relationship has not yet been worked out.

As human milk in some communities may constitute an important exposure source for methylmercury, the implications for nursing practices should be considered. In this regard, the unquestionable benefits of nursing must be recognized (25). Thus, potential methylmercury exposures should preferably be prevented by means other than advising against breast-feeding, at least with regard to the first 6 months or so. Skerfving (5) recommended that both pregnant and lactating women should refrain from eating fish contaminated with methylmercury. However, for the individual consumer, fish high in mercury may not necessarily be easy to separate from fish that is safe, and a general warning against all seafood would seem difficult to defend. The health authorities in the Faroe Islands currently advise pregnant women to avoid eating pilot whale. As pilot whale is the main source of methylmercury exposure in the Faroes (14), the present study would suggest that this recommendation should also refer to the breast-feeding period. In communities where substantial mercury exposure from seafood is difficult to prevent by such recommendations or by pollution abatement, the prudence of prolonged nursing, i.e., beyond 6 months, may need to be considered.

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